REMARKS

A. Priority

It was asserted in the Office Action that the disclosure related specifically to cytochrome d (claim 5) does not have support to the January 21, 2000 filing date of U.S. Application No. 09/488,644 ("'644 Application"), while all other claims examined (claims 1-4 and 6-17) have that support. Office Action, page 3. Applicants respectfully disagree since cytochrome d was disclosed in the '644 Application, *e.g.*, *see* page 7, line 31-page 8, line 1. Reconsideration of this assertion is solicited.

B. Minor Objections to the Specification

The specification was objected to for lacking updated continuity data, insofar as the status of Application No. 09/488,644 was not up to date. Applicants have updated that status. The specification was objected to for a lack of a label for the description of the drawings and, allegedly, because the Applicants did not completely describe in the Abstract the subject matter disclosed in the Application. Applicants have provided the title to the description of the drawings, and they respectfully traverse the assertion that the Abstract did not completely describe the subject matter of the invention. Nonetheless, in the interest of expediting prosecution, the Abstract has been amended and it continues to satisfy all requirements of the patent statute and rules.

C. Claim Objections

Claim 5 has been amended by inserting the final period. This amendment overcomes the objection of claim 5.

Claim 13 was objected as allegedly being of improper dependent form, insofar as it failed to further limit the subject matter of a previous claim. Applicants were advised

to either cancel the claim(s), amend the claim(s), to place it (or them) in proper dependent form or rewrite the claim(s) in independent form. Office Action, page 4.

Applicants respectfully traverse this objection. Claim 13 is directed to a starter culture composition which comprises the modified lactic acid bacterial cell of claim 1. Claim 1 is directed to a modified lactic acid bacterial cell that includes at least 0.1 ppm on a dry matter basis of a porphyrin compound. Thus, the subject matter of claim 1 is directed to cells, while claim 13 is directed to a starter culture composition. Claim 13 adds the further limitation, i.e., "a starter culture composition," which is absent from claim 1. Reconsideration and withdrawal of this objection is solicited.

D. Claim Rejections Under 35 U.S.C. § 112, 2nd paragraph

Claims 1-17 were rejected under 35 U.S.C. § 112, 2nd paragraph as being indefinite, for failure to particularly point out and distinctly claim the subject matter regarded by Applicants as their invention. The rejection was based on the use of the term "culturally modified," which was alleged to be unclear. Office Action, page 5. It was elaborated that because the specification describes lactic acid bacteria treated with porphyrin in a culture and which, when placed in a porphyrin-free culture, retain particular characteristics induced by the porphyrin exposure, it is necessary that the porphyrin-induced characteristics in the absence of porphyrin can be induced in the cell only by some form of genetic mutation. This, according to the text of the Office Action, appears to be inconsistent with an assertion that the invention does not involve genetic engineering or classical mutagenesis. It was suggested that the claim be amended to a lactic acid bacteria culture previously treated in a culture with a particular porphyrin concentration, then removed from the porphyrin culture and placed in a different culture where the bacteria has certain characteristics. *Id.*

Applicants also respectfully traverse this rejection.

Initially, Applicants traverse the assertion in the Office Action that a specific genetic alteration is likely to explain the effect discovered by Applicants in the bacteria subjected to treatment with porphyrin. As stated in the specification, Applicants discovered that known lactic acid bacteria cells can be modified to decrease their NOX activity and their LDH activity by subjecting the cells to altered growing conditions. In particular, a known lactic acid bacterial culture containing lactic acid bacterial cells is subjected to a treatment with a substrate which contains porphyrin, the cells are thereafter removed from the substrate and placed in a different substrate, where they exhibit their altered characteristics with respect to the NOX and LDH activities.

Furthermore, section 112, 2nd paragraph requires claims to be definite, which has been interpreted to mean that the claims must apprise those skilled in the art of the metes and bounds of Applicants' claimed invention. Applicants' specification defines a "culturally modified lactic acid bacterial cell" as a cell of a lactic acid bacterium which has been cultured by fermentation in an appropriate nutrient medium containing an effective amount of at least one porphyrin compound. See specification, page 6, lines 4-7. The term "an effective amount" is also defined in the same paragraph to mean "an amount that is sufficient to cause the lactic acid bacterium to become modified", as defined in the specification. This definition clearly informs persons of ordinary skill in the art of the subject matter of Applicants' claims 1-17 with the requisite precision.

Nonetheless, in the interest of expediting prosecution, Applicants amended claim 1, which continues to be definite.

E. Claims 3-5 Are Definite

Claims 3-5 were rejected as indefinite because, allegedly, the "detectable amount" was not clear without recitation of a detection method. It was stated that without "definition of the detection methods, the required limitation of an amount of the cytochrome is unclear." Office Action, page 5. Applicants respectfully traverse this rejection because claims 3-5, as originally drafted, also apprised persons of ordinary skill in the art of the metes and bounds of the invention. Nonetheless, in the interest of expediting prosecution, Applicants cancelled claim 3 and amended claims 4 and 5 to be dependent from claim 1. Claims 4 and 5 continue to be definite.

F. Claims 7 and 17

Claims 7 and 17 were rejected as indefinite due to the presence of the term "including". Applicants amended claims 7 and 17 and added two new claims, 34 and 35, based on the original claims 7 and 17. Claims 7 and 17 continue to be definite.

G. Claims 8 and 9

Claims 8 and 9 were alleged to be indefinite because the term "about" in reference to temperature indicates an unclear breadth of the temperature. Office Action, page 6. Applicants respectfully submit that the term "about" is commonly used in patent law and it adds breadth to a limitation which it modifies. The extent of the additional breadth is determined based on the knowledge of persons of ordinary skill in the art. In the context of Applicants' invention, the term "about" means that the scope of the recited temperature is expanded by two degrees, i.e., 28-32 degrees. Thus, Applicants' claims 8 and 9 are definite and withdrawal of this rejection is respectfully solicited.

H. Claims 10-12

These claims were also alleged to be indefinite because of the presence of the abbreviation "NOX" and "LDH". It was suggested that the terms should be replaced with "NADH oxidase (NOX)" and "lactate dehydrogenase (LDH)" for clarity. Office Action, page 6. Applicants respectfully point out that the abbreviations originally present in claims 10-12 are well known to those skilled in the art, as indicated by the text of the Office Action. Nonetheless, in the interest of expediting prosecution, Applicants have amended claims 10-12, as suggested by the Examiner.

I. Original Claims 1-17 Satisfied the Written Description Requirement: Amended Claims Continue to Do So

Claims 1-17 were rejected under 35 U.S.C. 112, first paragraph, allegedly because they contained subject matter not described in the specification in such a manner as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed. It was asserted that claim 1 was directed to lactic acid bacteria that are claimed solely by function and without any structural limitations.

The Federal Circuit decision, *University of California v. Eli Lilly & Co.*, 1997 U.S. App., Lexis 18221 at 223, 43 USPQ.2d 1398 (Fed. Cir. 1997) was cited for the proposition that "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as b[y] structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Office Action, page 7. It was additionally explained that to fully describe a genus of a genetic material which is a chemical compound, applicants "must (1) fully describe at least one species of the claimed genus sufficient to represent said

genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these." *Id.*

Further, it was asserted that Applicants in their specification described lactic acid bacteria, specifically (according to the text of the Office Action) *L. lactis* subsp. lactis, treated in culture with porphyrin (specifically, haemin). *Id.* It was additionally asserted that the NOX and LDH activities of such bacteria are affected and their cytochrome d content, which alters their oxygen consumption even after the bacteria are placed in a different porphyrin-free culture. It was further said that specific genetic alterations to explain such effects are likely but not described, and asserted that no structure of the claimed bacteria was described. It was concluded in the Office Action that a single species of the claimed genus is described in the specification without description of any common structural characteristics, so that a person of skill in the art could ascertain the structure of other genus members. Office Action, pages 7-8.

Applicants respectfully traverse this rejection.

Applicants concede that their claim 1 is directed to a lactic acid bacterial cell. They also agree, in principle, with the summary of a few selected (out of context) portions of the Federal Circuit *Lilly* opinion. Nonetheless, the Federal Circuit in *Lilly* also stated that ". . . where no explicit description of a generic invention is to be found in the specification . . . mention of representative compounds may provide an implicit description upon which to base generic claim language", and " . . . it may not be

necessary to enumerate a plurality of species if a genus is sufficiently identified in an application by 'other appropriate language'". 43 U.S.P.Q. at 1406.

In their application Applicants define the term "lactic acid bacteria" as

> a group of Gram positive, catalase negative, non-motile, microaerophilic or anaerobic bacteria which ferment sugar with the production of acids including lactic acid as the predominantly produced acid, acetic acid, formic acid and propionic acid. The industrially most useful lactic acid bacteria are found among *Lactococcus* species, *Lactobacillus* species, *Streptococcus* species, *Enterococcus* species, *Leuconostoc* species, *Oenococcus* species and *Pediococcus* species.

This definition is well known in the art and satisfies the description requirement of 35 U.S.C. § 112, 1st paragraph, insofar as it defines the claimed subject matter by a well-recognized name in the industry ("lactic acid bacteria") exemplified by a number of species. This definition satisfies the first requirement set forth at page 7 of the Office Action ("fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus"). The description of the function of the genus and its characteristics (i.e., "ferment sugar with the production of acids including lactic acid as the predominantly produced acid, acetic acid, formic acid and propionic acid" -- specification, page 1, line 26), satisfies the second stated requirement ("identify the common characteristics of the claimed molecules, e.g., . . . physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these"). Office Action, page 7.

The properties of lactic acid bacteria, which include their function, identified above, are both well known in the art and identified in the specification. It is also well

known in the art and identified in the specification that the functional characteristics are coupled with structure of the bacteria. This is further illustrated by the working examples in the application which are directed to a specific strain of *Lactoccus lactis* subsp. *lactis* CHCC373 (Experiment 1, beginning at page 18) and a mixed strain starter culture of *Lactoccus lactis* strains (Experiment 2, beginning at page 26).

Thus, Applicants have provided the disclosure of a number of representative species falling within the claimed genus, thereby satisfying the written description requirement of the statute as held by the Federal Circuit in *Lilly*.

Claim 7 was separately rejected under 35 U.S.C. § 112, 1st paragraph, as directed to a non-enabled subject matter because the requirement to enable such a deposit of species identified by the accession number DSM 12015 must contain a statement certifying the removal of all restrictions on accessibility to the deposit when the patent is granted. Office Action, page 8. Applicants submit herewith a Declaration of Deposit Under the Budapest Treaty which states the removal of all such restrictions.

J. Applicants' Claims Are Patentable Over Kaneko , *et al.* and Geppel, *et al.*

Claims 1, 6, 7, 10, 11, 13-15 and 17 were rejected under 35 U.S.C. § 102(b) as anticipated by Kaneko, *et al.* Acetoin Fermentation by Citrate-Positive *Lactococcus lactis* subsp. *lactis* 3022 Grown Aerobically in the Presence of Hemin or Cu^{2+}, Applied and Environmental Microbiology, September 1990, Vol. 56, No. 9:2644-2649. It was stated that Kaneko *et al.* teach *Lactoccus lactis* subsp. *lactis* 3022 citrate-positive cells grown in 6.5 mg/L hemin, a porphyrin compound. According to the Office Action, the cells have 75 percent of the NOX activity of those not treated with hemin. Table 3 on page 1648 of Kaneko *et al.* was relied upon for this assertion. It was stated that the culture is liquid and contains bacterial nutrients and that the dry weight of the cells (2.27

mg/ml) inherently falls within the CFU strains claimed as a starter culture. Office Action, page 9.

Applicants respectfully submit that their claims, prior to their amendment herein, were not anticipated by Kaneko, *et al.* Nonetheless, in the interest of expediting prosecution, Applicants amended their claims. The amended claims continue to be patentable. Claim 1, the only independent claim in the set of claims being examined, is directed to a modified lactic acid bacterial cell which has been treated with a porphyrin-containing substrate so that the cell contains at least 0.1 ppm on a dry matter basis of a porphyrin compound.

It is well established that the Patent Office has the burden of establishing *prima facie* case of unpatentability of Applicants' claimed invention. To establish anticipation of the claimed invention, the Patent Office must identify a reference disclosing every single limitation of rejected claims arranged in the same order as in the claims. Kaneko *et al.* fail to meet all of the claimed limitations. For example, Kaneko *et al.* do not disclose that their cells have a particular content of porphyrin, much less the herein-claimed at least 0.1 ppm of porphyrin. It was conceded in the Office Action that Kaneko *et al.* "do not teach that their cells have at least 0.1 ppm porphyrin", but it was alleged that this feature was inherent in Kaneko *et al.*'s composition because of the treatment of the cells, which is the same as disclosed in Geppel *et al.* (WO01/52668). Office Action, pages 9-10. It was alleged that Table 4 on page 25 of Geppel *et al.* shows inherently the presence of haemin, a porphyrin compound, in the cells of Kaneko *et al.* to the concentrations required by Applicants' claims. *Id.* This was based on the assertion that Kaneko *et al.*'s teaching of aerobic propagation of cells of a certain species (*Lactoccus*

lactis subsp. *lactis* 3022) in 6.5 mg/L haemin is the same process as taught by Geppel *et al.* to treat a different strain of *Lactoccus lactis* subsp. *lactis* at 10 mg/L haemin, which evidences many of the characteristics inherent in the cells taught by Kaneko *et al.* Office Action, page 9.

Applicants respectfully traverse this basis for the assertion that Kaneko *et al.*'s disclosure inherently teaches lactic acid bacterial cells containing 0.1 ppm of porphyrin or more. As an initial matter, this assertion is inconsistent with the statement in the Office Action that "Kaneko *et al.* do not teach their cells have at least 0.1 ppm porphyrin ...", Office Action, page 9, last paragraph. Applicants concur with this statement.

Furthermore, as correctly pointed out by the Examiner, the concentration of haemin in Geppel *et al.*'s nutrient medium is 10 mg/L, which is approximately 54% higher than the 6.5 mg/L concentration taught by Kaneko *et al.* The Patent Office has provided no reasonable scientific basis for asserting that such a substantially lower concentration of haemin would inherently produce the same result as taught by Geppel *et al.* For at least this reason, Applicants respectfully submit that claims 1, 6, 7, 10, 11, 13-15 and 17 are patentable in view of Kaneko *et al.*

Furthermore, Kaneko *et al.* fail to anticipate some of the dependent claims because they fail to disclose (expressly or inherently) the limitations of such dependent claims. For example, claim 15 requires a composition comprising 10^4 - 10^{12} CFU per gram of viable modified lactic acid bacterial cells of claim 1. Claim 17 additionally requires the presence in the composition of at least one component enhancing the

viability of the bacterial cell during storage. These limitations are not disclosed by Kaneko *et al.*

K. Claims 2-5, 8, 9 and 12 Are Patentable Over Kaneko, *et al.* in View of Geppel, *et al.*

Claims 2-5, 8, 9 and 12 were rejected under 35 U.S.C. § 102(b) as anticipated by Kaneko *et al.* as evidenced by Geppel *et al.* This rejection was premised on the assertion (discussed to some extent above) that Geppel *et al.* teach a treatment similar to that of Kaneko *et al.* of a different strain of *Lactoccus lactis* subsp. *lactis* with 10 mg/L of haemin, as compared to 6.5 mg/L of haemin. It was concluded that the claimed features of the 0.1 ppm content of cytochrome d, in Applicants' claims, increased oxygen consumption under particular conditions (claims 8-9) and decreased LDH activity by at least 10% (claim 12) are inherent in the cells of Kaneko *et al.* because Geppel *et al.*'s procedure is very similar to that of Kaneko *et al.* Office Action, pages 9-10.

Applicants respectfully traverse this rejection. As pointed out above, the concentration of haemin in Geppel *et al.* is more than 50% greater than in Kaneko *et al.* In view of such a substantially greater content of haemin in the treatment of Geppel *et al.*, it is unreasonable to conclude that a cell produced by the method of Geppel *et al.* will have the same cytochrome d content and other properties (discussed above) as that of Kaneko *et al.*

A prior art disclosure can be properly used in an inherency-based anticipation rejection only if the disclosure always and inevitably produces the asserted (yet not explicitly disclosed) result. The significant difference in the haemin content between

Kaneko *et al.* and Geppel *et al.* supports Applicants' assertion that Kaneko *et al.*'s cells do not have the same content of haemin as those of Applicants' claimed invention.

Furthermore, some of the dependent claims contain additional limitations which further distinguish them from the disclosure of Kaneko *et al.* For example, claim 8 requires that the cell, when it is in the form of a cell suspension is inoculated in the specified concentration (10^7 cells/ml) into low pasteurized skimmed milk having a specified amount of dissolved oxygen (8 ppm) and left standing in the milk for a specified period of time (2 hours at the temperature of about 30° C.), the cell consumes at least 25% of the oxygen. Claim 9 requires that the amount of the dissolved oxygen consumed by the cell be at least 50% and claim 12 specifies that the cell has LDH activity decreased by at least 10%. None of these limitations is disclosed (explicitly or inherently) by Kaneko *et al.*

For at least the reasons set forth above, Applicants submit that claims 2-5, 8, 9 and 12 are also patentable in view of Kaneko *et al.*

Additionally, it was conceded in the Office Action that Geppel *et al.* is not prior art to Applicants' application at least because Applicants claim priority from Geppel *et al.* Nonetheless, it was asserted that "the critical date of extrinsic evidence showing a universal fact need not antedate the filing date". Office Action, page 10.

Applicants respectfully traverse the implied assertion that Geppel *et al.* show a "universal fact" which implicitly had been known in prior art. Geppel *et al.* is Applicants' invention and the disclosure of Geppel *et al.* evidences the fact that Applicants were the first to discover unusual and unexpected results obtained when a lactic acid bacterial

cell is treated in accordance with Applicants' invented method. Prior to Applicants' discovery, neither the method nor its product were known in the art.

V. Request for Allowance

An indication of allowance of all claims is solicited. In the event any issues are outstanding, Applicants would appreciate the courtesy of a telephone call to the undersigned counsel to resolve such issues in an expeditious manner and place the application in condition for allowance.

It is believed that all necessary fees are enclosed. However, if any additional fees are determined to be due, the Commissioner is hereby authorized to charge these fees to the undersigned's Deposit Account No. 50-0206.

Respectfully submitted,

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